Schistosomiasis: Health Effects on Women

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Schistosomiasis is a parasitic infection endemic in 74 resource-poor nations that affects approximately 200 million people. Schistosomes are water-borne flatworms or blood flukes that enter the human body through the skin. Some symptoms of schistosomiasis include fever, arthralgias, abdominal pain, bloody diarrhea, and hematuria. Ultimately, patients develop heptosplenomegaly, ascites, and lymphadenopathy. Schistosomiasis is a neglected tropical disease, and its global health impact is grossly underestimated. Women suffer considerably from female genital schistosomiasis that causes infertility, preterm labor, anemia, menstrual disorders, and dyspareunia. More effort is needed to prevent schistosomiasis. Treating pregnant and lactating women decreases the disease burden and improves maternal and fetal outcome.
[Rev Obstet Gynecol. *2010;3(1):28-32 doi: 10.3909/riog0109*]

Key words: Schistosomiasis • Praziquantel • Female genital schistosomiasis

Schistosomiasis, also known as, bilharzia, bilharziasis, or snail fever, affects approximately 200 million people worldwide. Theodor Bilharz, a German surgeon who worked in Cairo, discovered schistosomiasis in 1851. Today, 120 million people are symptomatic.[1] Over 80% of the disease is currently found in sub-Saharan Africa (Figure 1). According to the World Health Organization (WHO), approximately 652 million people are at risk with an estimated 200,000 deaths occurring annually. Forty million women of childbearing age are infected.[2] WHO has placed schistosomiasis as the third most devastating tropical disease, following malaria and intestinal helminthiasis.[3]

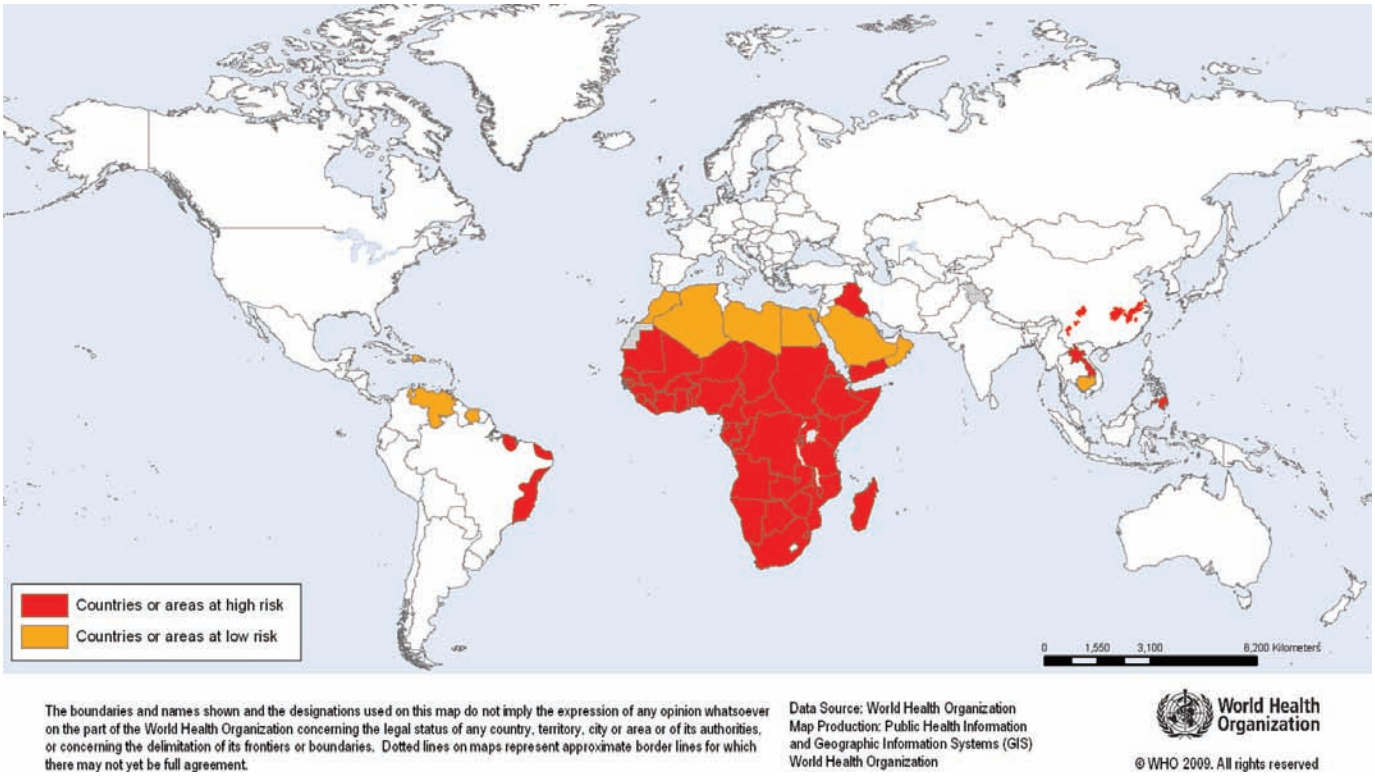

Figure 1. *Countries and areas at risk for schistosomiasis (2008). Available at http://gamapserver.who.int/mapLibrary/Files/Maps/Global_ShistoPrevalence_ITHRiskMap.png. Reprinted with permission.*

There are 5 species of schistosomiasis. These water-borne flatworms or blood flukes are schistosomes. The most common are *Schistosoma mansoni, S japonicum,* and *S haematobium*. The rarer forms are *S intercalatum* and *S mekongi*. *S mansoni* occurs in Africa, the Caribbean, South America, and the Eastern Mediterranean. *S japonicum* and *S mekongi* are found in Southeast Asia and the Western Pacific. *S intercalatum* is endemic in central Africa and *S haematobium* occurs throughout Africa and the Eastern Mediterranean. *S haematobium* affects both the urinary and reproductive tract systems, whereas the 4 other species impact the hepatic and gastrointestinal systems.[4]

Who Is at Risk?

Schistosomiasis, like many tropical diseases, is endemic in areas where poor living conditions and poverty are prevalent. Because these are water-borne species, populations that primarily rely on agriculture and fishing for their livelihood are at the highest risk of contamination. Often, individuals in these regions are also co-infected with other parasitic diseases such as malaria and hook worm. Women and children (peaking at age 10 to 19 years) are at high risk. Children play in water and women use water for their daily chores.[4] Given the increased migration from rural to urban regions, the disease is spreading to urban areas and infecting swimmers. Due to increased ecotourism, the cases of schistosomiasis are being diagnosed more often in travelers.

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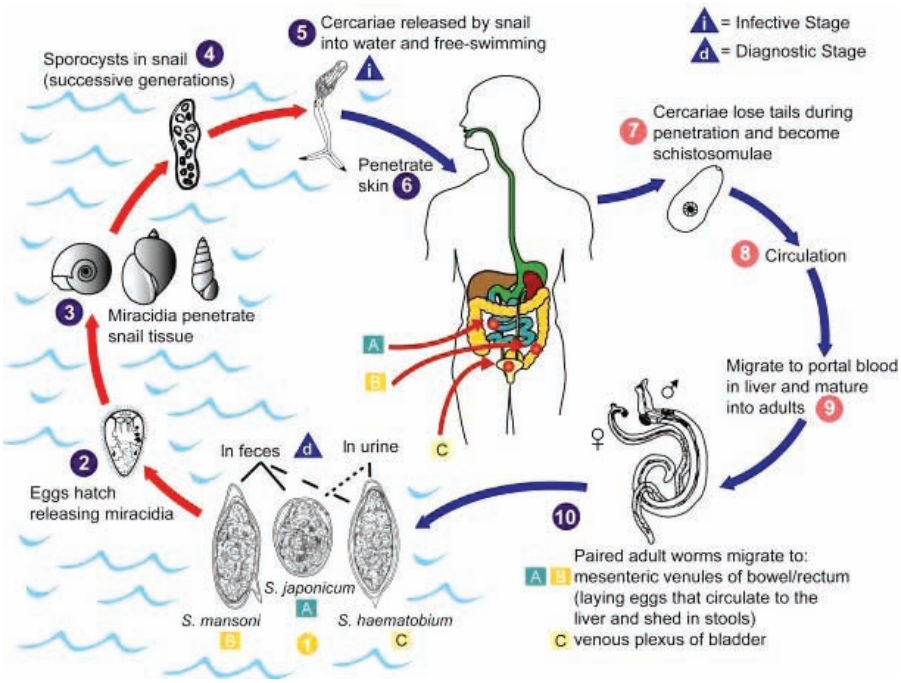

Figure 2. *Lifecycle of schistosomiasis. Available at http://med.stanford.edu/labs/michael-hsieh/images/Schistosomiasis_Life_Cycle.jpg. Reprinted with permission.*

Lifecycle

The lifecycle of schistosomes begins from the miracidia that are excreted in human feces or urine into fresh water (Figure 2). The miracidia have 1 to 3 weeks to search for their intermediate host—a snail. The infected snail eventually excretes the larva form, called cercaria. The two-tailed cercariae swim until they reach a human host and burrow through intact skin using oral suckers (Figure 3).

The cercariae lose their tail upon entry and transform into schistosomulae that develop a double-lipid barrier that is resistant to human immune responses. They incorporate host proteins and major histocompatibility complexes and migrate through blood vessels. They enter pulmonary capillaries and eventually enter the portal veins where they mature into adult worms. Male and female worms attach together at the male's gynecophoric canal (Figure 4). Here they migrate into mesenteric veins (*S mansoni, S japonicum*) or vesicular veins (*S haematobium*).

Figure 3. *Cercariae. Available at http://www.abdn.ac.uk/ibes/research/int_phys/vector/. Reprinted with permission.*

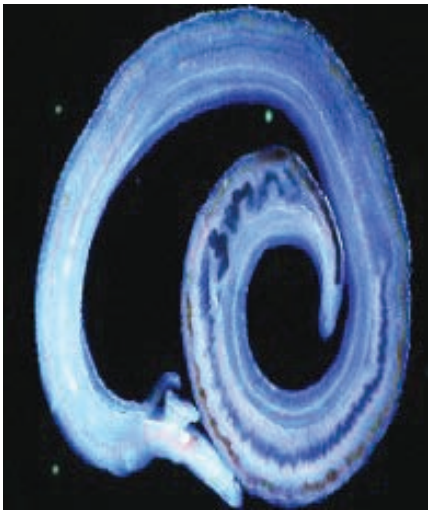

Figure 4. *Male and female worm paired. Available at http://www.blessedherbs.com/images/pck-09.jpg. Reprinted with permission.*

Eggs are released into the bowel or bladder and cause a granulomatous response. During this time, they mature into miracidia that are excreted out of the human host via urine or feces, thus completing the cycle.[5]

Symptoms

Most people do not develop symptoms of acute schistosomiasis. Individuals who have had prior infections are most likely to develop high temperatures known as Katayama fever. Although symptoms resolve after a few weeks, mortality rates can be as high as 25% during this acute phase. A maculopapular rash appears at the site of entry. Those with prior exposure to schistosomiasis can develop a significant schistosomal dermatitis (Figure 5). Laboratory findings show increased eosinophilia and circulating immune complexes.

In the chronic stage, symptoms can present months or years later. They vary depending on the species that has infected the host. In general, the eggs induce a significant immune response and form granulomas. *S mansoni* and *S japonicum* cause abdominal pain, bloody diarrhea, and colonic polyposis. Eggs that remain in the portal system develop periportal fibrosis. Symptoms include portal hypertension, hematemesis, ascites, splenomegaly, and esophageal variceal bleeding.

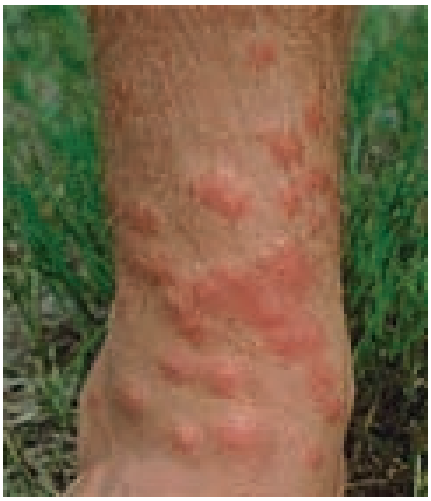

Figure 5. *Maculopapular rash. Available at http://www.stanford.edu/group/parasites/ParaSites2006/Schistosomiasis/dermat.jpg. Reprinted with permission.*

Granulomatosis in the pulmonary system leads to chronic coughs, palpitations, atypical chest pain, pulmonary hypertension, cor pulmonale, and ultimately death.[5]

S haematobium deposit their eggs in the urinary tract system. Symptoms include dysuria, hematuria, bladder polyps, ulcers, obstructive uropathies, and squamous cell bladder cancer. Women manifest female genital schistosomiasis (discussion below). Eggs can end up in the skin, brain, muscle, adrenal glands, and eyes. In some cases, severe symptoms such as seizures, mental status changes, and even paralysis can occur. Coinfection of schistosomiasis along with other diseases such as hepatitis, human immunodeficiency virus, and malaria can raise the risk for hepatocellular carcinoma and increase the risk of mortality.[5]

Laboratory Diagnosis

Urinary schistosomiasis can be diagnosed either grossly or microscopically. With the use of a microscope, paper, polycarbonate, or nylon filters, hematuria can be identified. Cellophane soaked in glycerine detects the eggs of the schistosomiasis taken from fecal samples. Fecal samples are also useful in diagnosing mesenteric disease. Microscopic egg counts can help determine the infection load. Serologically, an elevated eosinophilia is useful to diagnose an acute event, whereas elevated liver and renal function tests indicate chronic disease involving those organs. Serologically, an enzyme-linked immunosorbent assay test can diagnose exposure but it does not distinguish between active or inactive infection.

Treatment and Prevention

Praziquantel (PZQ) effectively treats all forms of schistosomiasis. It only requires 2 to 3 doses for 1 day. Although it has minimal side effects, it cannot prevent future infections. In the acute phase, especially in cases where the egg infestation is high, PZQ may worsen symptoms. Patients who become severely ill may need corticosteroids to decrease the inflammatory response. The recovery rate is as high as 98%.[5]

Perhaps the most effective way to decrease schistosomiasis is through prevention. Interventions that focus on mass treatments of PZQ (without diagnosis) decrease the prevalence of this disease. In some cases, mass treatment has reduced the infection rate by 15%.[6] PZQ is both inexpensive and the 1-day-only therapy makes these interventions easy to implement and successful. However, there appears to be a growing resistance to PZQ. Other initiatives such as improving sanitation, making social and behavioral changes regarding hygiene, targeting the snail host, and developing a vaccine have been challenging.

Female Genital Schistosomiasis

Female genital schistosomiasis (FGS) is predominantly caused by *S haematobium*. During their reproductive years, women suffer severe morbidity and mortality because of FGS. As the eggs penetrate the urinary system, they can find their way to the female genital region and form granulomas in the uterus, fallopian tube, and ovaries. Women develop uterine enlargement, menstrual disorders, cervicitis, and infertility. Externally, vulvar or perianal lesions develop in 30% of women. These lesions appear ulcerated, hypertrophic, or even fistulous.

Schistosomiasis also affects the uterine environment during pregnancy. Approximately, 10 million women in Africa have schistosomiasis in pregnancy.[2] Studies have demonstrated that pregnant women infected with schistosomiasis develop severe anemia, have low birth weight infants, and an increased infant and maternal mortality rate.[2,6-9] Schistosomiasis has been detected in the placenta and newborns have been diagnosed with the disease, thus confirming congenital infection. Data suggest that infected women have a higher rate of spontaneous abortions and a higher risk for ectopic pregnancies.[10,11]

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Since 1979, pregnant and lactating women had not been treated with PZQ, the main line of therapy. In 2002, after assessing data from animals and pregnant women who inadvertently received PZQ, the WHO stated that PZQ was indeed recommended in pregnancy. This significantly changed the morbidity rate of

women. Women whose treatment was delayed because of pregnancy and lactation suffered more severe and chronic disease, leading to end organ damage. In addition, the increased pelvic blood flow during pregnancy is thought to assist in accelerating the disease and increasing the infection load. Recent studies have determined the safety and efficacy of PZQ in pregnancy.[2,12] Despite WHO's recommendations and these studies, Ministries of Health have been cautious in implementing them.

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Conclusions

Schistosomiasis has been a neglected tropical disease and, as a result, little attention has been paid to women with FGS. Given the safety, efficacy, and low cost of PZQ, programs are continuing large-scale periodic treatment of at-risk populations without diagnosis. Special attention must be given to pregnant and lactating women to decrease the disease burden and improve pregnancy and fetal outcomes. Prevention of this disease must occur during adolescence because transmission is common due to children swimming in contaminated waters. If programs can target this population, the likelihood of improving women's reproductive life and well-being will be directly affected. ■

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Main Points

- According to the World Health Organization (WHO), approximately 652 million people are at risk for schistosomiasis with an estimated 200,000 annual deaths. Forty million women of childbearing age are infected and the WHO has placed schistosomiasis as the third most devastating tropical disease, following malaria and intestinal helminthiasis.
- In chronic schistosomiasis, symptoms can present months or years later and can vary depending on the species that has infected the host. In general, the eggs induce a significant immune response and form granulomas. *Schistosoma mansoni* and *S japonicum* cause abdominal pain, bloody diarrhea, and colonic polyposis. Granulomatosis in the pulmonary system leads to chronic coughs, palpitations, atypical chest pain, pulmonary hypertension, cor pulmonale, and ultimately death.
- Praziquantel (PZQ) effectively treats all forms of schistosomiasis, is inexpensive, and only requires 2 to 3 doses for 1 day. Although it has minimal side effects, it cannot prevent future infections.
- Female genital schistosomiasis (FGS) is predominantly caused by *S haematobium*. Women suffer severe morbidity and mortality during their reproductive years due to FGS. As the eggs penetrate the urinary system, they migrate to the female genital region and form granulomas in the uterus, fallopian tube, and ovaries, leading to the development of uterine enlargement, menstrual disorders, cervicitis, and infertility.
- The most effective way to decrease the spread of schistosomiasis is through prevention. Interventions that focus on mass treatments of PZQ (without diagnosis) decrease the prevalence of this disease, and in some cases, mass treatment has reduced the infection rate by as much as 15%.